	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	72	clostridial adj neurotoxin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/27 14:53			0
2	BRS	L2	393	botulinum adj toxin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/27 14:53			0
3	BRS	L3	69	clostridial adj toxin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/27 14:53			0
4	BRS	L4	179	target adj moiety	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/27 14:54			0
5	BRS	L5	136	transmission adj compound	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/27 14:55			0
6	BRS	L6	3846	substance adj P	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/27 14:55			0
7	BRS	L7	1	(5 or 6) same 4	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/27 14:56			0
8	BRS	L9	1	8 same (expressing or expression)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/27 14:58			0
9	BRS	L10	1	8 same (genetic adj construct)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/27 14:58			0
10	BRS	L8	19	(1 or 2 or 3) same (4 or 5 or 6)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/27 15:09			0
11	BRS	L11	956	targeting adj moiety	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/27 15:09			0
12	BRS	L12	20	(1 or 2 or 3) same 11	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/07/27 15:10			0

> d his

(FILE 'HOME' ENTERED AT 15:13:59 ON 27 JUL 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
15:14:25 ON 27 JUL 2002
L1 1256 S CLOSTRIDIAL (W) (NEUROTOXIN OR TOXIN)
L2 16906 S BOTULINUM TOXIN
L3 0 S CLOSTRIDIAL (W) (BERATTI OR BUTYRICUM OR TATANI)
L4 1 S CLOSTRIDIAL (W) (BERATTI OR BUTYRICUM OR TETANI)
L5 17834 S L1 OR L2 OR L4
L6 607 S (TARGET? MOIETY) OR (TRANSMISSION COMPOUND)
L7 94664 S SUBSTANCE P
L8 53 S L5 (P) (L6 OR L7)
L9 24 DUPLICATE REMOVE L8 (29 DUPLICATES REMOVED)
L10 14 S L8 (P) (EXPRESS? OR RECOMBINANT OR GENETIC CONSTRUCT)
L11 3 DUPLICATE REMOVE L10 (11 DUPLICATES REMOVED)
L12 21 S L9 NOT L11

=> log y

=> d his

(FILE 'HOME' ENTERED AT 15:27:42 ON 27 JUL 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
15:28:13 ON 27 JUL 2002
L1 17833 S (CLOSTRIDIAL TOXIN) OR (CLOSTRIDIAL NEUROTOXIN) OR (BOTULINUM
L2 94674 S (SUBSTANCE P) OR (TRANSMISSION COMPOUND)
L3 4 S L1 (P) L2 (P) (CONJUGATE OR FUSION PROTEIN)
L4 4 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)

=> log y

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FILE 'HOME' ENTERED AT 15:13:59 ON 27 JUL 2002

=> file medline caplus biosis embase scisearch agricola
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 15:14:25 ON 27 JUL 2002

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FILE 'AGRICOLA' ENTERED AT 15:14:25 ON 27 JUL 2002

=> s clostridial (w) (neurotoxin or toxin)
L1         1256 CLOSTRIDIAL (W) (NEUROTOXIN OR TOXIN)

=> s botulinum toxin
L2        16906 BOTULINUM TOXIN

=> s clostridial (w) (beratti or butyricum or tatani)
L3            0 CLOSTRIDIAL (W) (BERATTI OR BUTYRICUM OR TATANI)

=> s clostridial (w) (beratti or butyricum or tetani)
L4            1 CLOSTRIDIAL (W) (BERATTI OR BUTYRICUM OR TETANI)

=> s l1 or l2 or l4
L5        17834 L1 OR L2 OR L4

=> s (target? moiety) or (transmission compound)
L6          607 (TARGET? MOIETY) OR (TRANSMISSION COMPOUND)

=> s substance P
L7        94664 SUBSTANCE P

=> s l5 (p) (l6 or l7)
L8           53 L5 (P) (L6 OR L7)

=> duplicate remove l8
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L8
L9            24 DUPLICATE REMOVE L8 (29 DUPLICATES REMOVED)

=> s l8 (p) (express? or recombinant or genetic construct)
L10           14 L8 (P) (EXPRESS? OR RECOMBINANT OR GENETIC CONSTRUCT)

=> duplicate remove l10
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L10
L11            3 DUPLICATE REMOVE L10 (11 DUPLICATES REMOVED)

=> d l11 1-3 ibib abs

L11  ANSWER 1 OF 3     MEDLINE                          DUPLICATE 1
ACCESSION NUMBER:    2001325272     MEDLINE
DOCUMENT NUMBER:     21218317   PubMed ID: 11320861
TITLE:               [Botulinum toxin A for the treatment of headache disorders
```

and pericrani[redacted] pain syndromes].
Botulinum-Tox[redacted] A in der Therapie von Kopfschmerzerkrankungen und perikranialen Schmerzsyndromen.
AUTHOR: Gobel H; Heinze A; Heinze-Kuhn K; Austermann K
CORPORATE SOURCE: Neurologisch-verhaltensmedizinische Schmerzklinik Kiel in Kooperation mit der Universitat Kiel, Heikendorfer Weg 9-27, 24149 Kiel.. kiel@Schmerzklinik.de
SOURCE: NERVENARZT, (2001 Apr) 72 (4) 261-74. Ref: 104
Journal code: 0400773. ISSN: 0028-2804.
PUB. COUNTRY: Germany: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010611
Last Updated on STN: 20010611
Entered Medline: 20010607

AB For 20 years ***botulinum*** ***toxin*** A has been used for the treatment of a variety of disorders characterised by pathologically increased muscle contraction. Recently, treatment of tension headache, migraine, cluster headache, and myofascial pain syndromes of neck, shoulder girdle, and back with ***botulinum*** ***toxin*** A has become a rapidly expanding new field of research. Several modes of action are discussed for these indications. The blockade of cholinergic innervation reduces muscular hyperactivity for 3 to 6 months. Degenerative changes in the musculoskeletal system of the head and neck are prevented. Nociceptive afferences and blood vessels of the pericranial muscles are decompressed and muscular trigger points and tender points are resolved. The normalisation of muscle spindle activity leads to a normalisation of muscle tone and central control mechanisms of muscle activity. Oromandibular dysfunction is eliminated and muscular stress removed. However, the effect of ***botulinum*** ***toxin*** A cannot be explained by muscular actions only. Its retrograde uptake into the central nervous system modulates the ***expression*** of ***substance*** ***P*** and enkephalins in the spinal cord and nucleus raphe. Recent findings suggest an inhibition of sterile inflammation which may lead to a blockade of the neurogenic inflammation believed to be the pathophysiological substrate of primary headache disorders. The efficacy of ***botulinum*** ***toxin*** A in the treatment of pain disorders is being investigated in several studies at the moment. The results and experiences obtained so far present new alternatives in the treatment of chronic pain disorders. The practical use of ***botulinum*** ***toxin*** A is demonstrated.

L11 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000148594 MEDLINE
DOCUMENT NUMBER: 20148594 PubMed ID: 10683301
TITLE: Enkephalin and aFGF are differentially regulated in rat spinal motoneurons after chemodenervation with botulinum toxin.
AUTHOR: Humm A M; Pabst C; Lauterburg T; Burgunder J M
CORPORATE SOURCE: Laboratory of Neuromorphology, University of Berne, Berne, CH3010, Switzerland.
SOURCE: EXPERIMENTAL NEUROLOGY, (2000 Jan) 161 (1) 361-72.
Journal code: 0370712. ISSN: 0014-4886.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000330
Last Updated on STN: 20000330
Entered Medline: 20000323

AB ***Botulinum*** ***toxin*** is used to induce transient graded paresis by chemodenervation in the treatment of focal hyperkinetic movement disorders. While the molecular events occurring in motoneurons after mechanical nerve lesioning leading to muscle paresis are well known, they have been investigated to a lesser extent after chemodenervation. We therefore examined the ***expression*** of enkephalin (ENK), acidic fibroblast growth factor (aFGF), neurotensin (NT), galanin (GAL),

substance ***P*** (SP), vasoactive intestinal polypeptide (VIP), and neuropeptide Y (NPY) in rat spinal motoneurons after chemodenervation of the gastrocnemius. In order to precisely localize the motoneurons targeting the injection site, retrograde tracing was performed in additional rats by using Fluorogold injections. ENK ***expression*** was upregulated in the region corresponding to the Fluorogold positive motoneurons, but also on the contralateral side and in more distant parts of the spinal cord. The highest upregulation occurred 7 to 14 days after injections and decreased over a period of three months. At 8 days, aFGF was slightly downregulated in all regions studied, single motoneurons showed NT ***expression*** , while ***expression*** of GAL, SP, VIP, and NPY could be detected neither in controls nor in toxin-treated animals. These alterations in gene ***expression*** were strikingly different from those described after axotomy. Our present findings give additional demonstration of the considerable plasticity of the adult spinal cord after ***botulinum*** ***toxin*** treatment.

L11 ANSWER 3 OF 3 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 97078373 MEDLINE
DOCUMENT NUMBER: 97078373 PubMed ID: 8919297
TITLE: Effect of muscle denervation on the expression of substance P in the ventral raphe-spinal pathway of the rat.
AUTHOR: Van den Bergh P; De Beukelaer M; Deconinck N
CORPORATE SOURCE: Laboratoire de Biologie Neuromusculaire, Service de Neurologie, Cliniques Universitaires St-Luc, Universite de Louvain, Brussels, Belgium.
SOURCE: BRAIN RESEARCH, (1996 Jan 29) 707 (2) 206-12.
Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970407
Last Updated on STN: 20000407
Entered Medline: 19970327

AB The medullary raphe nuclei, wherein serotonin (5-HT) coexists with ***substance*** ***P*** (SP) and thyrotropin-releasing hormone (TRH), innervate lower motor neurons in the spinal cord ventral horn by means of the ventral raphe-spinal pathway. Destruction of the ventral raphe-spinal pathway is associated with deficient recovery of denervated muscle, indicating that it may exert a trophic effect upon lower motor neurons. To determine whether SP could be a trophic factor for lower motor neurons within the ventral raphe-spinal pathway, the effect of muscle denervation with ***botulinum*** ***toxin*** type A on SP-encoding beta-preprotachykinin mRNA in the rat medullary raphe was examined by in situ hybridization histochemistry. Silver grain density over hybridized medullary raphe neurons was increased by up to 11%, although the number of hybridized neurons did not change in denervated as compared to control rats. Increased SP gene ***expression*** in the medullary raphe in response to motor unit lesioning suggests that raphe-spinal SP may be trophic to lower motor neurons.

=> d his

(FILE 'HOME' ENTERED AT 15:13:59 ON 27 JUL 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 15:14:25 ON 27 JUL 2002

L1	1256	S CLOSTRIDIAL (W) (NEUROTOXIN OR TOXIN)
L2	16906	S BOTULINUM TOXIN
L3	0	S CLOSTRIDIAL (W) (BERATTI OR BUTYRICUM OR TATANI)
L4	1	S CLOSTRIDIAL (W) (BERATTI OR BUTYRICUM OR TETANI)
L5	17834	S L1 OR L2 OR L4
L6	607	S (TARGET? MOIETY) OR (TRANSMISSION COMPOUND)
L7	94664	S SUBSTANCE P
L8	53	S L5 (P) (L6 OR L7)
L9	24	DUPLICATE REMOVE L8 (29 DUPLICATES REMOVED)
L10	14	S L8 (P) (EXPRESS? OR RECOMBINANT OR GENETIC CONSTRUCT)
L11	3	DUPLICATE REMOVE L10 (11 DUPLICATES REMOVED)

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=> s l9 not l11
L12         21 L9 NOT L11

=> d l12 1-21 ibib abs

L12  ANSWER 1 OF 21     MEDLINE
ACCESSION NUMBER:   2002216275     IN-PROCESS
DOCUMENT NUMBER:    21948777   PubMed ID: 11952288
TITLE:              Adjuvant botulinum toxin A in dyshidrotic hand eczema: a
                    controlled prospective pilot study with left-right
                    comparison.
AUTHOR:             Wollina U; Karamfilov T
CORPORATE SOURCE:   Department of Dermatology and Allergology, the
                    Friedrich-Schiller-University of Jena, Germany..
                    Wollina-Uw@khdf.de
SOURCE:             JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY AND
                    VENEREOLOGY, (2002 Jan) 16 (1) 40-2.
                    Journal code: 9216037. ISSN: 0926-9959.
PUB. COUNTRY:       Netherlands
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE:         Entered STN: 20020416
                    Last Updated on STN: 20020416
AB   OBJECTIVE: Dyshidrotic hand eczema is a therapeutic challenge. A
     prospective pilot study was performed with left-right comparison in order
     to investigate whether chemical de-innervation of sudoriferic nerves would
     be superior to standard therapy with topical corticosteroids. BACKGROUND:
       ***Botulinum***     ***toxin***   A (BTXA) is a potent inhibitor of
     acetylcholine release, that induces eccrine sweat production and release.
     Inhibition of sweating by other measures such as tap water iontophoresis
     has been shown to be beneficial in dyshidrotic hand eczema. METHODS: Eight
     adult patients suffering from dyshidrotic hand eczema (atopic type) were
     included in a prospective, side-by-side controlled clinical pilot study
     using topical corticosteroids on both hands in combination with
     intracutaneous injections of 100 units of BTXA (Botox) on the more
     severely affected hand on day 1. The dyshidrotic hand eczema was
     classified using the DASI (Dyshidrotic Eczema Area and Severity Index)
     before treatment (0), after 1 week, 4 weeks and 8 weeks. RESULTS: Six
     patients completed the study, two dropped out because of social and
     personal reasons. The mean DASI score changed from 28 to17 with topical
     therapy alone and from 36 to 3 with adjuvant BTXA (P < 0.01). Itching and
     vesiculation were inhibited earlier when using the combination of
     corticosteroids and BTXA. There was one relapse in the corticosteroid
     group. Relapses have not been seen in the BTXA group. CONCLUSIONS:
     Interruption of sweating by BTXA improves the outcome and reduces relapses
     in patients with dyshidrotic hand eczema. BTXA is antipruritic as well
     suggesting that it does not only interact with acetylcholine release but
       ***substance***     ***p***  .

L12  ANSWER 2 OF 21     MEDLINE
ACCESSION NUMBER:   2001680312     MEDLINE
DOCUMENT NUMBER:    21583314   PubMed ID: 11727162
TITLE:              [Early pain reduction in the treatment of spasticity after
                    a single injection of botulinum A toxin].
                    Fruhe Schmerzreduktion in der Therapie von Spastik nach
                    einmaliger Botulinustoxin-A-Injektion.
AUTHOR:             Chalkiadaki A; Rohr U P; Hefter H
CORPORATE SOURCE:   Neurologische Klinik, Heinrich-Heine-Universitat,
                    Dusseldorf.. chalkiadaki@med.uni-duesseldorf.de
SOURCE:             DEUTSCHE MEDIZINISCHE WOCHENSCHRIFT, (2001 Nov 30) 126 (48)
                    1361-4.
                    Journal code: 0006723. ISSN: 0012-0472.
PUB. COUNTRY:       Germany: Germany, Federal Republic of
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           German
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200201
ENTRY DATE:         Entered STN: 20011203
                    Last Updated on STN: 20020125
                    Entered Medline: 20020107
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AB HISTORY,.ADMISSION FINDINGS AND DIAGNOSIS: After stem-cell transplantation a 45-year-old woman (case 1) had an attack of general hypoxia requiring resuscitation. She then developed a quadriplegia and spasticity of all limbs notably of the right arm and a severe pain syndrome which had to be treated by oral and intravenous analgesics. Immobilisation and secondary complications aggravated the already difficult situation. In the 2nd case a 66-year-old woman was admitted to our outpatient clinic with long-standing left-sided spastic hemiparesis after territorial infarction of the right middle cerebral artery. Beside the spasticity she also suffered from a distinct pain syndrome which did not respond to any oral analgesics. TREATMENT AND COURSE: For the treatment of the main symptoms, both patients received intramuscular injections of 1000 MU ***botulinum*** ***toxin*** A (Dysport(R) Ipsen Pharma). Astonishingly, both patients experienced pain relief the next day, whereas spasticity started to respond only 5-6 days later. CONCLUSIONS: In our experience pain relief after ***botulinum*** ***toxin*** A injections occurs not only due to reduced muscle hyperactivity, especially when such a temporal dissociation between pain relief and muscle relaxation appears as in the two cases reported above. Rather, we believe that ***botulinum*** ***toxin*** A interferes with the release of other neurotransmitters e. g. ***substance*** ***P*** (SP) and calcitonine-gene-related-peptide (CGRP) having a key function in the nociceptive cascade.

L12 ANSWER 3 OF 21 MEDLINE
ACCESSION NUMBER: 2001410068 MEDLINE
DOCUMENT NUMBER: 21228699 PubMed ID: 11329944
TITLE: Presynaptic effects of botulinum toxin type A on the neuronally evoked response of albino and pigmented rabbit iris sphincter and dilator muscles.
AUTHOR: Ishikawa H; Mitsui Y; Yoshitomi T; Mashimo K; Aoki S; Mukuno K; Shimizu K
CORPORATE SOURCE: Department of Ophthalmology Kitasato University, School of Medicine, 1-15-1 Kitasato, Sagamihara, 228-8555, Japan.
SOURCE: NIPPON GANKA GAKKAI ZASSHI. ACTA SOCIETATIS OPHTHALMOLOGICAE JAPONICAE, (2001 Apr) 105 (4) 218-22. Journal code: 7505716. ISSN: 0029-0203.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719
AB PURPOSE: To investigate the effects of ***botulinum*** ***toxin*** type A(botulinum A toxin) on the autonomic and other non-adrenergic, non-cholinergic nerve terminals. METHODS: The effects of neurotoxin on twitch contractions evoked by electrical field stimulation (EFS) were studied in isolated rabbit iris sphincter and dilator muscles using isometric tension recording. RESULTS: Botulinum A toxin(150 nM) inhibited the fast cholinergic and slow ***substance*** ***P*** -ergic component of contraction evoked by EFS in the rabbit iris sphincter muscle without affecting the response to carbachol and ***substance*** ***P*** . Botulinum A toxin(150 nM) did not affect the twitch contraction evoked by EFS in the rabbit iris dilator muscle. CONCLUSION: These data indicated that botulinum A toxin may inhibit not only the acetylcholine release in the cholinergic nerve terminals, but also ***substance*** ***P*** release from the trigeminal nerve terminals of the rabbit iris sphincter muscle. However, neurotoxin has little effect on the adrenergic nerve terminals of the rabbit iris dilator muscle.

L12 ANSWER 4 OF 21 MEDLINE
ACCESSION NUMBER: 2001325277 MEDLINE
DOCUMENT NUMBER: 21218322 PubMed ID: 11320866
TITLE: [Reduction of pain and muscle spasms by botulinum toxin A]. Reduktion von Schmerzen und Muskelanspannung durch Botulinum-Toxin A.
AUTHOR: Kelm S; Gerats G; Chalkiadaki A; Hefter H
CORPORATE SOURCE: Neurologische Klinik der Heinrich-Heine-Universitat Dusseldorf, Moorenstr. 5, 40225 Dusseldorf.. Stefan.Kelm@uni-duesseldorf.de

SOURCE: NERVENARZT, (2001 Apr) 72 (4) 302-6.
Journal code: 400773. ISSN: 0028-2804.
PUB. COUNTRY: Germany: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010611
Last Updated on STN: 20010611
Entered Medline: 20010607

AB ***Botulinum*** ***toxin*** A (BoNT-A) develops its muscle-relaxing effect by the inhibition of acetylcholine (ACh) release. This toxin is also known to relieve muscular pain in different disorders. Conspicuously, pain in some patients responds earlier and sometimes even better than muscle tension, indicating that the effect of BoNT-A on pain is not only due to inhibition of ACh release. A questionnaire was distributed to 88 patients suffering from cervical dystonia (CD). Thirty-five completed questionnaires could be used for data analysis. After intramuscular injections of BoNT-A, patients with CD experience significant reductions in pain which sometimes occur significantly earlier than the improvements in head posture. In the iris sphincter muscle of the rabbit and in dorsal root ganglion cells (DRG) of the rat, inhibition of the release of ***substance*** ***P*** by BoNT-A has been shown experimentally, and BoNT-C has been proven to develop endopeptidase activity toward ***substance*** ***P*** (SP) in vitro. Findings in the current literature and our observations allow the conclusion that alleviation of muscle pain by BoNT-A may also be due to an effect on the release of nociceptive neuropeptides, among which SP seems to have a key function.

L12 ANSWER 5 OF 21 MEDLINE
ACCESSION NUMBER: 2000464599 MEDLINE
DOCUMENT NUMBER: 20470451 PubMed ID: 11019785
TITLE: A conjugate composed of nerve growth factor coupled to a non-toxic derivative of Clostridium botulinum neurotoxin type A can inhibit neurotransmitter release in vitro.
AUTHOR: Chaddock J A; Purkiss J R; Duggan M J; Quinn C P; Shone C C; Foster K A
CORPORATE SOURCE: Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire, UK.
SOURCE: GROWTH FACTORS, (2000) 18 (2) 147-55.
Journal code: 9000468. ISSN: 0897-7194.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010202

AB Nerve growth factor (NGF) receptor binding, internalisation and transportation of NGF has been identified as a potential route of delivery for other molecules. A derivative of Clostridium botulinum neurotoxin type A (LHN) that retains catalytic activity but has significantly reduced cell-binding capability has been prepared and chemically coupled to NGF. Intact ***clostridial*** ***neurotoxins*** potently inhibit neurotransmitter release at the neuromuscular junction by proteolysis of specific components of the vesicle docking/fusion complex. Here we report that the NGF-LHN/A conjugate, when applied to PC12 cells, significantly inhibited neurotransmitter release and cleaved the type A toxin substrate. This work represents the successful use of NGF as a ***targeting*** ***moiety*** for the delivery of a neurotoxin fragment.

L12 ANSWER 6 OF 21 MEDLINE
ACCESSION NUMBER: 2000181909 MEDLINE
DOCUMENT NUMBER: 20181909 PubMed ID: 10715374
TITLE: Presynaptic effects of botulinum toxin type A on the neuronally evoked response of albino and pigmented rabbit iris sphincter and dilator muscles.
AUTHOR: Ishikawa H; Mitsui Y; Yoshitomi T; Mashimo K; Aoki S; Mukuno K; Shimizu K
CORPORATE SOURCE: Department of Ophthalmology, Kitasato University, School of

Medicine, Sag[illegible]ihara, Japan.
SOURCE: JAPANESE JOUR[illegible]L OF OPHTHALMOLOGY, (2000 Mar-A[illegible] 44 (2) 106-9.
Journal code: 0044652. ISSN: 0021-5155.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000616
Last Updated on STN: 20000616
Entered Medline: 20000606

AB PURPOSE: To investigate the effects of ***botulinum*** ***toxin*** type A (botulinum A toxin) on the autonomic and other nonadrenergic, noncholinergic nerve terminals. METHODS: The effects of botulinum A toxin on twitch contractions evoked by electrical field stimulation (EFS) were studied in isolated albino and pigmented rabbit iris sphincter and dilator muscles using the isometric tension recording method. RESULTS: Botulinum A toxin inhibited the fast cholinergic and slow ***substance*** ***P*** -ergic component of the contraction evoked by EFS in the rabbit iris sphincter muscle without affecting the response to carbachol and ***substance*** ***P*** . These inhibitory effects were more marked in the albino rabbit than in the pigmented rabbit. Botulinum A toxin (150 nmol/L) did not affect the twitch contraction evoked by EFS in the rabbit iris dilator muscle. CONCLUSIONS: These data indicated that botulinum A toxin may inhibit not only the acetylcholine release in the cholinergic nerve terminals, but also ***substance*** ***P*** release from the trigeminal nerve terminals of the rabbit iris sphincter muscle. However, the neurotoxin has little effect on the adrenergic nerve terminals of the rabbit iris dilator muscle. Furthermore, the botulinum A toxin binding to the pigment melanin appears to influence the response quantitatively in the two types of irides.

L12 ANSWER 7 OF 21 MEDLINE
ACCESSION NUMBER: 82048151 MEDLINE
DOCUMENT NUMBER: 82048151 PubMed ID: 7296370
TITLE: BaCl2-induced contractions in the guinea pig ileum longitudinal muscle: role of presynaptic release of neurotransmitters and Ca2+ translocation in the postsynaptic membrane.
AUTHOR: Clement J G
SOURCE: CANADIAN JOURNAL OF PHYSIOLOGY AND PHARMACOLOGY, (1981 Jun) 59 (6) 541-7.
Journal code: 0372712. ISSN: 0008-4212.
PUB. COUNTRY: Canada
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198201
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 19970203
Entered Medline: 19820109

AB Early studies indicated that the baCl2-induced contractions in the guinea pig ileum longitudinal muscle strip (GPI-LMS) were, in part, neuronal in origin. However, recent studies have suggested that BaCl2-induced contractions were produced by an action directly on the smooth muscle membrane. The purpose of this study was to investigate the mechanism of the BaCl2 contractions in the GPI-LMS. ***Botulinum*** ***toxin*** (5 x 10(5) MLD/mL), which blocks the electrically induced release of acetylcholine (ACh), hemicholinium-3 (HC-3; 110 micro M), which blocks ACh synthesis, tetrodotoxin (TTX; 60 nM), which blocks Na+ channels, black widow spider venom, which depletes the presynaptic neuron of neurotransmitter, and atropine (2.9 micro M), a potent muscarinic antagonist, had no effect on the BaCl2 contractions. Densensitization of the GPI-LMS to ***substance*** ***P*** did not affect the BaCl2 contraction. In Ca2+ -free buffer the BaCl2 dose-response curve was shifted to the right. In Ca2+-free solution the time to 50% inhibiton of the contractile response to ACh (73 nM) and BaCl2 (1.16 mM) was 3.7 and 125 min, respectively. The D 600 Ic50 for ACh and BaCl2 contractions was 220 and 130 nM, respectively. In Ca2+-free buffer either EGTA (0.53 mM) or D 600 (1 micro M) were potent inhibitors of BaCl2 contractions. These results suggest that in the GPI-LMS the BaCl2 response is not mediated by

a release of ACh (or ***substance*** ***P***) because inhibitors of ACh release, synthesis, and receptors do not affect the responses. Also, the BaCl2 contraction is not due to activation of Na+ channels because TTX is without effect. The BaCl2-induced contraction appears to be mainly due to the movement of membrane bound Ca2+ through D 600 sensitive Ca2+ channels with extracellular Ca2+ and possible passage of Ba2+ ions intracellularly playing relatively minor roles.

L12 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:403839 CAPLUS
DOCUMENT NUMBER: 136:395977
TITLE: Clostridial toxin derivatives able to modify peripheral sensory afferent functions
INVENTOR(S): Foster, Keith Alan; Duggan, Michael John; Shone, Clifford Charles
PATENT ASSIGNEE(S): The Speywood Laboratory, Ltd., UK; Microbiological Research Authority
SOURCE: U.S., 18 pp., Cont.-in-part of U.S. Ser. No. 945,037. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6395513	B1	20020528	US 1999-447356	19991122
WO 9633273	A1	19961024	WO 1996-GB916	19960416
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 5989545	A	19991123	US 1998-945037	19980112

PRIORITY APPLN. INFO.: GB 1995-8204 A 19950421
WO 1996-GB916 A2 19960416
US 1998-945037 A2 19980112

AB The invention discloses an agent specific for peripheral sensory afferents. The agent may inhibit the transmission of signals between a primary sensory afferent and a projection neuron by controlling the release of at least one neurotransmitter or neuromodulator from the primary sensory afferent. The agent may be used in or as a pharmaceutical for the treatment of pain, particularly chronic pain. Agents of the invention include a modified ***clostridial*** ***neurotoxin*** fused to a ***targeting*** ***moiety*** . Prepn. and biol. testing of a conjugate of NGF with the LHN fragment of botulinum neurotoxin A are included.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:241331 CAPLUS
DOCUMENT NUMBER: 136:273210
TITLE: Clostridial toxin derivatives and methods for treating pain
INVENTOR(S): Donovan, Stephen
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U.S. Ser. No. 625,098. CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002037833	A1	20020328	US 2001-922093	20010803

PRIORITY APPLN. INFO.: US 2000-489667 A2 20000119
US 2000-625098 A2 20000725

AB Agents for treating pain, methods for producing the agents and methods for

treating pain by administration to a patient of a therapeutically effective amt. of the agent are disclosed. The agent can include a ***clostridial*** ***neurotoxin*** , or a component or fragment or deriv. thereof, attached to a ***targeting*** ***moiety*** , wherein the ***targeting*** ***moiety*** is selected from a group consisting of ***transmission*** ***compds*** . which can be released from neurons upon the transmission of pain signals by the neurons, and compds. substantially similar to the ***transmission*** ***compds*** . The agent comprises a ***botulinum*** ***toxin*** component covalently coupled to ***substance*** ***P*** .

L12 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:89857 CAPLUS
DOCUMENT NUMBER: 136:145260
TITLE: Clostridial toxin derivatives and methods for treating pain
INVENTOR(S): Donovan, Stephen
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002007759	A2	20020131	WO 2001-US21984	20010712

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-625098 A 20000725
AB Methods for treating a bone tumor, in particular pain assocd. with bone tumor, by administration to a patient of a therapeutically effective amt. of an agent are disclosed. The agent may include a ***clostridial*** ***neurotoxin*** component attached to a ***targeting*** ***moiety*** , wherein the ***targeting*** ***moiety*** is selected from the group consisting of ***transmission*** ***compds*** . which can be released from neurons upon the transmission of pain signals by the neurons, and compds. substantially similar to the ***transmission*** ***compds*** .

L12 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:762800 CAPLUS
DOCUMENT NUMBER: 135:322726
TITLE: A pharmaceutical composition containing a nicotine receptor agonist and an analgesic for treatment of acute, chronic pain and/or neuropathic pain and migraines
INVENTOR(S): Coe, Jotham Wadsworth; Harrigan, Edmund Patrick; O'Neill, Brian Thomas; Sands, Steven Bradley; Watsky, Eric Jacob
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001076576	A2	20011018	WO 2001-IB391	20010316
WO 2001076576	A3	20020620		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,

HR, HU, ID, IL, IN, [redacted], JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, [redacted], MK, MN, MW, MX, MZ, NO, NZ, [redacted], PT, RO,
RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2001036943 A1 20011101 US 2000-740307 20001218
PRIORITY APPLN. INFO.: US 2000-195738P P 20000407

AB Oral, parenteral or transdermal compns. are disclosed for the treatment of acute, chronic and/or neuropathic pain. The pharmaceutical compns. are comprised of a therapeutically effective combination of a nicotine receptor partial agonist and an analgesic agent and a pharmaceutically acceptable carrier. The analgesic agent is selected from opioid analgesics, NMDA antagonists, ***substance*** ***P*** antagonists, COX 1 and COX 2 inhibitors, tricyclic antidepressants (TCA), selective serotonin reuptake inhibitors (SSRI), capsaicin receptor agonists, anesthetic agents, benzodiazepines, skeletal muscle relaxants, migraine therapeutic agents, anticonvulsants, antihypertensives, antiarrhythmics, antihistamines, steroids, caffeine, N-type calcium channel antagonists and ***botulinum*** ***toxin*** . The method of using these compds. and a method of treating acute, chronic and/or neuropathic pain and migraine in a mammal including a human is also disclosed.

L12 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:545729 CAPLUS
DOCUMENT NUMBER: 135:132453
TITLE: ***Clostridial*** ***neurotoxin*** derivatives attached to ***targeting*** ***moieties*** , and methods using them for treating pain
INVENTOR(S): Donovan, Stephen
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001053336	A1	20010726	WO 2001-US1529	20010117

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002068699 A1 20020606 US 2001-938112 20010823
PRIORITY APPLN. INFO.: US 2000-489667 A 20000119

AB The invention provides agents for treating pain, methods for producing the agents, and methods for treating pain by administration to a patient of a therapeutically effective amt. of the agent. The agent can include a ***clostridial*** ***neurotoxin*** , or a component of fragment or deriv. thereof, attached to a ***targeting*** ***moiety*** , wherein the ***targeting*** ***moiety*** is selected from ***transmission*** ***compds*** . which can be released from neurons upon the transmission of pain signals by the neurons, and compds. substantially similar to the ***transmission*** ***compds*** .

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:228744 CAPLUS
DOCUMENT NUMBER: 134:247267
TITLE: Clostridial neurotoxin targeted conjugates for inhibition of secretion from non-neuronal cells
INVENTOR(S): Foster, Keith Alan; Chaddock, John Andrew; Purkiss, John Robert; Quinn, Conrad Padraig

PATENT ASSIGNEE(S): Microbiological Research Authority, UK
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021213	A2	20010329	WO 2000-GB3669	20000925

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-22554 A 19990923

AB A method of treatment of disease by inhibition of cellular secretory processes is provided. The method has particular application in the treatment of diseases dependent on the exocytotic activity of endocrine cells, exocrine cells, inflammatory cells, cells of the immune system, cells of the cardiovascular system, and bone cells. Agents and compns. therefor, as well as methods for manufg. these agents and compns., are provided. In a preferred embodiment a ***clostridial*** ***neurotoxin*** , substantially devoid of holotoxin binding affinity for neuronal cells of the presynaptic muscular junction, is assocd. with a ***targeting*** ***moiety*** . The ***targeting*** ***moiety*** is selected such that the ***clostridial*** ***toxin*** conjugate so formed may be directed to a non-neuronal target cell to which the conjugate may bind. Following binding, a neurotoxin component of the conjugate, which is capable of inhibition of cellular secretion, passes into the cytosol of the target cell by cellular internalization mechanisms. Thereafter, inhibition of secretion from the target cell is effected.

L12 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:323250 CAPLUS
DOCUMENT NUMBER: 132:303493
TITLE: Application of botulinum toxin to the management of neurogenic inflammatory disorders
INVENTOR(S): First, Eric R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6063768	A	20000516	US 1997-923884	19970904

PRIORITY APPLN. INFO.: US 1996-20400P P 19960906

AB A method is provided for the use of at least one serotype or a combination of serotypes of botulinum neurotoxin either alone or in combination with other peptides or fusion proteins, that when administered in a safe and effective amt., antagonize and therefore decrease or block inflammation induced by the neurogenic mechanisms underlying or assocd. with inflammatory disorders, in particular, arthritis.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:249106 CAPLUS
DOCUMENT NUMBER: 130:276767
TITLE: Conjugates of galactose-binding lectins and clostridial neurotoxins as analgesics
INVENTOR(S): Duggan, Michael John; Chaddock, John Andrew

PATENT ASSIGNEE(S): The Speywood Laboratory Limited, UK; Microbiological Research Authority
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9917806	A1	19990415	WO 1998-GB3001	19981007
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306350	AA	19990415	CA 1998-2306350	19981007
AU 9893574	A1	19990427	AU 1998-93574	19981007
AU 741456	B2	20011129		
ZA 9809138	A	19990527	ZA 1998-9138	19981007
EP 996468	A1	20000503	EP 1998-946571	19981007
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001518522	T2	20011016	JP 2000-514674	19981007

PRIORITY APPLN. INFO.: GB 1997-21189 A 19971008
WO 1998-GB3001 W 19981007

AB A class of novel agents that are able to modify nociceptive afferent function is provided. The agents may inhibit the release of neurotransmitters from discrete populations of neurons and thereby reduce or preferably prevent the transmission of afferent pain signals from peripheral to central pain fibers. They comprise a galactose-binding lectin linked to a deriv. of a clostridial neurotoxin. The deriv. of the clostridial neurotoxin comprises the L-chain, or a fragment thereof, which includes the active proteolytic enzyme domain of the light (L) chain, linked to a mol. or domain with membrane-translocating activity. The agents may be used in or as pharmaceuticals for the treatment of pain, particularly chronic pain.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:615391 CAPLUS
DOCUMENT NUMBER: 127:288483
TITLE: Capsaicin stimulates release of substance P from dorsal root ganglion neurons via two distinct mechanisms
AUTHOR(S): Purkiss, John R.; Welch, Mary J.; Doward, Sarah; Foster, Keith A.
CORPORATE SOURCE: CAMR (Centre of Applied Microbiology and Research), Salisbury, Wiltshire, SP4 0JG, UK
SOURCE: Biochemical Society Transactions (1997), 25(3), 542S
CODEN: BCSTB5; ISSN: 0300-5127
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this report, the authors describe both extracellular Ca2+-dependent and -independent mechanisms of capsaicin-induced release of ***substance*** ***P*** from cultured embryonic rat dorsal root ganglion neurons. Further, the authors describe the differing ***botulinum*** ***toxin*** A sensitivity of these two mechanisms. Rat dorsal root ganglion neurons (DRGs) were prepd. from 14-16 days gestation embryos. Release of ***substance*** ***P*** was measured and then total ***substance*** ***P*** was measured following capsaicin or KCl stimulation in the absence of Ca2+ and in the presence of Ca2+. ***Substance*** ***P*** immunoreactivity was measured using an enzyme immunoassay kit. Botulinum neurotoxin (BoNT/A) cleavage of SNAP-25 was measured in cells following 18-20 h exposure to toxin. From the results the authors found that capsaicin is able to evoke release of

substance ***P*** from DRGs by two mechanisms. The first mechanism is Ca2+-dependent, maximally stimulated by 0.3.mu.M capsaicin and requires intact SNAP-25 for optimum release. The second mechanism is Ca2+-independent, becomes activated at 3-10.mu.M capsaicin and is insensitive to BoNT/A so it induces release through a mechanism that does not have SNAP-25 as an essential component.

L12 ANSWER 17 OF 21 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:251745 BIOSIS
DOCUMENT NUMBER: PREV200100251745
TITLE: Neuronal plasticity in various neuropathic pain model mice.
AUTHOR(S): Ueda, Hiroshi (1)
CORPORATE SOURCE: (1) Department of Molecular Pharmacology and Neuroscience, Nagasaki University School of Pharmaceutical Sciences, Nagasaki Japan
SOURCE: Neuroscience Research Supplement, (2000) No. 24, pp. S7. print.
Meeting Info.: 23rd Annual Meeting of the Japan Neuroscience Society and the 10th Annual Meeting of the Japanese Neural Network Society Yokohama, Japan September 04-06, 2000
ISSN: 0921-8696.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L12 ANSWER 18 OF 21 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:256755 BIOSIS
DOCUMENT NUMBER: PREV200000256755
TITLE: Enhanced ***Substance*** ***P*** response of ***botulinum*** ***toxin*** -injected opossum lower esophageal sphincter.
AUTHOR(S): Gaumnitz, Eric A. (1); Bass, Paul; Osinski, Mark A.
CORPORATE SOURCE: (1) Univ of Wisconsin Med Sch, Madison, WI USA
SOURCE: Gastroenterology, (April, 2000) Vol. 118, No. 4 Suppl. 2 Part 1, pp. A154. print..
Meeting Info.: 101st Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week. San Diego, California, USA May 21-24, 2000 American Gastroenterological Association
. ISSN: 0016-5085.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L12 ANSWER 19 OF 21 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1976:180040 BIOSIS
DOCUMENT NUMBER: BA62:10040
TITLE: CONTRACTION AND RELAXATION OF THE RETRACTOR PENIS MUSCLE AND PENILE ARTERY OF THE BULL A STUDY OF EFFECTS OF DRUGS AND TRANS MURAL NERVE STIMULATION ON ISOLATED SMOOTH MUSCLE STRIPS.
AUTHOR(S): KLINGE E; SJOSTRAND N O
SOURCE: ACTA PHYSIOL SCAND SUPPL, (1974 (RECD 1975)) (420), 1-88.
CODEN: APSSAD. ISSN: 0302-2994.
FILE SEGMENT: BA; OLD
LANGUAGE: Unavailable
AB The effects of field stimulation and various endogenous compounds and drugs on autonomic nerves or receptors were investigated on isolated strips of the retractor penis muscle and the penile artery of the bull. Excitatory and inhibitory responses to field stimulation and secondary contraction were abolished by tetrodotoxin or local anesthetic drugs. The excitatory response to field stimulation was inhibited or abolished by .alpha.-adrenoceptor and adrenergic neuron blocking agents and was enhanced by inhibitors of neuronal noradrenaline uptake. Noradrenaline and adrenaline contracted the retractor penis and the penile artery. This effect was abolished by .alpha.-adrenoceptor blocking agents. After .alpha.-receptor blockade adrenaline, noradrenaline and isoprenaline produced relaxation which was prevented by .beta.-adrenoceptor blocking agents. The inhibitory response to field stimulation was not prevented by antimuscarinic, ganglionic blocking or neuromuscular blocking drugs or counteracted by ***botulinum*** ***toxin*** or hemicholinium and

was apparently unaffected by physostigmine. It was uncovered by adrenergic neuron blocking agents. Acetylcholine caused contraction of the smooth muscle, suppression of the excitatory response to field stimulation and a brief relaxation sometimes preceded by a rapid contraction and resembling the effect of transmural nerve stimulation. The first 2 effects of acetylcholine were emulated by pilocarpine and prevented by antimuscarinic drugs; the 3rd effect was prevented by hexamethonium and emulated by nicotine. Nicotine-induced relaxations were prevented by ganglionic blocking agents and by local anesthetics. All acetylcholine effects, particularly the last, required high concentrations. Histamine and 5-hydroxytryptamine contracted both penis and artery. The inhibitory response to field stimulation were not blocked by antihistamines or serotonin antagonists. ATP contracted the penis but relaxed the penile artery. Desensitization to ATP abolished or reversed this relaxation, but had no effect on the inhibitory response to field stimulation. No overt effects on the retractor penis and penile artery were obtained with .gamma. aminobutyric acid [GABA], glycine, glutamic acid, aspartic acid or several other amino acids. Prostaglandins (PG) E1 and E2 relaxed the retractor penis; PGF2.alpha. contracted it. All were powerful stimulants of arterial smooth muscle. Prolonged exposure to inhibitors of PG synthesis did not suppress inhibitory responses to field stimulation. Minute concentrations of bradykinin contracted the retractor penis but had almost no effect on the penile artery. ***Substance*** ***P*** contracted the muscles. Posterior pituitary hormones had no overt effect on the retractor penis but contracted the penile artery.

L12 ANSWER 20 OF 21 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2000:530062 SCISEARCH
THE GENUINE ARTICLE: 309RU
TITLE: Enhanced ***substance*** ***P*** response of ***botulinum*** ***toxin*** -injected opossum lower esophageal sphincter.
AUTHOR: Gaumnitz E A (Reprint); Bass P; Osinski M A
CORPORATE SOURCE: UNIV WISCONSIN, SCH PHARM, MADISON, WI; UNIV WISCONSIN, SCH MED, MADISON, WI; UNIV WISCONSIN, SCH PHARM, MADISON, WI
COUNTRY OF AUTHOR: USA
SOURCE: GASTROENTEROLOGY, (APR 2000) Vol. 118, No. 4, Part 1, Supp. [2], pp. 889-889.
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399.
ISSN: 0016-5085.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L12 ANSWER 21 OF 21 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 1999:910001 SCISEARCH
THE GENUINE ARTICLE: 257VL
TITLE: Sensitivity of embryonic rat dorsal root ganglia neurons to Clostridium botulinum neurotoxins
AUTHOR: Welch M J; Purkiss J R (Reprint); Foster K A
CORPORATE SOURCE: PUBL HLTH LAB SERV, CTR APPL MICROBIOL & RES, SALISBURY SP4 0JG, WILTS, ENGLAND (Reprint); PUBL HLTH LAB SERV, CTR APPL MICROBIOL & RES, SALISBURY SP4 0JG, WILTS, ENGLAND
COUNTRY OF AUTHOR: ENGLAND
SOURCE: TOXICON, (FEB 2000) Vol. 38, No. 2, pp. 245-258.
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.
ISSN: 0041-0101.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 34
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Clostridium botulinum neurotoxins (BoNT) are zinc dependent endopeptidases which. once internalised into the neuronal cytosol, block neurotransmission :by proteolysis of membrane-associated proteins putatively involved in synaptic vesicle docking and fusion with the plasma membrane. Although many studies have used a variety of cellular systems to study the neurotoxins, most require relatively large amounts of toxin dr

permeabilisation to internalise the neurotoxin. We present here a primary culture of embryonic rat dorsal root ganglia (DRG) neurons that exhibits calcium-dependent substance P secretion when depolarised with elevated extracellular potassium and is naturally BoNT sensitive. The DRG neurons showed a different IC50 for each of the toxins tested with a 1000 fold difference between the most and least potent neurotoxins (0.05, 0.3,30 and similar to 60 nM for A, C, F and B, respectively). BoNT/A cleavage of SNAP-25 was seen as early as 2 h, but substance P secretion was not significantly inhibited until 4 h intoxication and the effects of BoNT/A were observed for as long as 15 days. This primary neuronal culture system represents a new and sensitive cellular model for the ill vitro study of the botulinum neurotoxins. (C) 1999 Elsevier Science Ltd. All rights reserved.

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=> d his

     (FILE 'HOME' ENTERED AT 15:13:59 ON 27 JUL 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     15:14:25 ON 27 JUL 2002
L1          1256 S CLOSTRIDIAL (W) (NEUROTOXIN OR TOXIN)
L2         16906 S BOTULINUM TOXIN
L3             0 S CLOSTRIDIAL (W) (BERATTI OR BUTYRICUM OR TATANI)
L4             1 S CLOSTRIDIAL (W) (BERATTI OR BUTYRICUM OR TETANI)
L5         17834 S L1 OR L2 OR L4
L6           607 S (TARGET? MOIETY) OR (TRANSMISSION COMPOUND)
L7         94664 S SUBSTANCE P
L8            53 S L5 (P) (L6 OR L7)
L9            24 DUPLICATE REMOVE L8 (29 DUPLICATES REMOVED)
L10           14 S L8 (P) (EXPRESS? OR RECOMBINANT OR GENETIC CONSTRUCT)
L11            3 DUPLICATE REMOVE L10 (11 DUPLICATES REMOVED)
L12           21 S L9 NOT L11

=> log y
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                82.64      82.85

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                -5.58      -5.58

STN INTERNATIONAL LOGOFF AT 15:21:08 ON 27 JUL 2002
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=> d his

(FILE 'HOME' ENTERED AT 15:13:59 ON 27 JUL 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
15:14:25 ON 27 JUL 2002
L1 1256 S CLOSTRIDIAL (W) (NEUROTOXIN OR TOXIN)
L2 16906 S BOTULINUM TOXIN
L3 0 S CLOSTRIDIAL (W) (BERATTI OR BUTYRICUM OR TATANI)
L4 1 S CLOSTRIDIAL (W) (BERATTI OR BUTYRICUM OR TETANI)
L5 17834 S L1 OR L2 OR L4
L6 607 S (TARGET? MOIETY) OR (TRANSMISSION COMPOUND)
L7 94664 S SUBSTANCE P
L8 53 S L5 (P) (L6 OR L7)
L9 24 DUPLICATE REMOVE L8 (29 DUPLICATES REMOVED)
L10 14 S L8 (P) (EXPRESS? OR RECOMBINANT OR GENETIC CONSTRUCT)
L11 3 DUPLICATE REMOVE L10 (11 DUPLICATES REMOVED)
L12 21 S L9 NOT L11

=> log y

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FILE 'HOME' ENTERED AT 15:27:42 ON 27 JUL 2002

=> file medline caplus biosis embase scisearch agricola
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 15:28:13 ON 27 JUL 2002

FILE 'CAPLUS' ENTERED AT 15:28:13 ON 27 JUL 2002
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FILE 'EMBASE' ENTERED AT 15:28:13 ON 27 JUL 2002
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FILE 'SCISEARCH' ENTERED AT 15:28:13 ON 27 JUL 2002
COPYRIGHT (C) 2002 Institute for Scientific Information (ISI) (R)

FILE 'AGRICOLA' ENTERED AT 15:28:13 ON 27 JUL 2002

=> s (clostridial toxin) or (clostridial neurotoxin) or (botulinum toxin)
L1        17833 (CLOSTRIDIAL TOXIN) OR (CLOSTRIDIAL NEUROTOXIN) OR (BOTULINUM
                TOXIN)

=> s (substance p) or (transmission compound)
L2        94674 (SUBSTANCE P) OR (TRANSMISSION COMPOUND)

=> s l1 (p) l2 (p) (conjugate or fusion protein)
L3            4 L1 (P) L2 (P) (CONJUGATE OR FUSION PROTEIN)

=> duplicate remove l3
PROCESSING COMPLETED FOR L3
L4             4 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)

=> d l4 1-4 ibib abs

L4   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:89857  CAPLUS
DOCUMENT NUMBER:          136:145260
TITLE:                    Clostridial toxin derivatives and methods for treating
                          pain
INVENTOR(S):              Donovan, Stephen
PATENT ASSIGNEE(S):       Allergan Sales, Inc., USA
SOURCE:                   PCT Int. Appl., 67 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   3
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2002007759      A2   20020131       WO 2001-US21984  20010712
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
             RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
             VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                    US 2000-625098   A  20000725
AB   Methods for treating a bone tumor, in particular pain assocd. with bone
     tumor, by administration to a patient of a therapeutically effective amt.
```

of an agent are disclosed. The agent may include a clostridial neurotoxin component attached to a targeting moiety, wherein the targeting moiety is selected from the group consisting of transmission compds. which can be released from neurons upon the transmission of pain signals by the neurons, and compds. substantially similar to the transmission compds.

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:241331 CAPLUS
DOCUMENT NUMBER: 136:273210
TITLE: Clostridial toxin derivatives and methods for treating pain
INVENTOR(S): Donovan, Stephen
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U.S. Ser. No. 625,098.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002037833	A1	20020328	US 2001-922093	20010803

PRIORITY APPLN. INFO.: US 2000-489667 A2 20000119
US 2000-625098 A2 20000725

AB Agents for treating pain, methods for producing the agents and methods for treating pain by administration to a patient of a therapeutically effective amt. of the agent are disclosed. The agent can include a clostridial neurotoxin, or a component or fragment or deriv. thereof, attached to a targeting moiety, wherein the targeting moiety is selected from a group consisting of transmission compds. which can be released from neurons upon the transmission of pain signals by the neurons, and compds. substantially similar to the transmission compds. The agent comprises a botulinum toxin component covalently coupled to substance P.

L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:545729 CAPLUS
DOCUMENT NUMBER: 135:132453
TITLE: Clostridial neurotoxin derivatives attached to targeting moieties, and methods using them for treating pain
INVENTOR(S): Donovan, Stephen
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001053336	A1	20010726	WO 2001-US1529	20010117
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002068699	A1	20020606	US 2001-938112	20010823

PRIORITY APPLN. INFO.: US 2000-489667 A 20000119

AB The invention provides agents for treating pain, methods for producing the agents, and methods for treating pain by administration to a patient of a therapeutically effective amt. of the agent. The agent can include a clostridial neurotoxin, or a component of fragment or deriv. thereof, attached to a targeting moiety, wherein the targeting moiety is selected from transmission compds. which can be released from neurons upon the transmission of pain signals by the neurons, and compds. substantially

similar to the transmission cmpds.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:249106 CAPLUS
DOCUMENT NUMBER: 130:276767
TITLE: Conjugates of galactose-binding lectins and clostridial neurotoxins as analgesics
INVENTOR(S): Duggan, Michael John; Chaddock, John Andrew
PATENT ASSIGNEE(S): The Speywood Laboratory Limited, UK; Microbiological Research Authority
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9917806	A1	19990415	WO 1998-GB3001	19981007
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306350	AA	19990415	CA 1998-2306350	19981007
AU 9893574	A1	19990427	AU 1998-93574	19981007
AU 741456	B2	20011129		
ZA 9809138	A	19990527	ZA 1998-9138	19981007
EP 996468	A1	20000503	EP 1998-946571	19981007
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001518522	T2	20011016	JP 2000-514674	19981007

PRIORITY APPLN. INFO.: GB 1997-21189 A 19971008
WO 1998-GB3001 W 19981007

AB A class of novel agents that are able to modify nociceptive afferent function is provided. The agents may inhibit the release of neurotransmitters from discrete populations of neurons and thereby reduce or preferably prevent the transmission of afferent pain signals from peripheral to central pain fibers. They comprise a galactose-binding lectin linked to a deriv. of a clostridial neurotoxin. The deriv. of the clostridial neurotoxin comprises the L-chain, or a fragment thereof, which includes the active proteolytic enzyme domain of the light (L) chain, linked to a mol. or domain with membrane-translocating activity. The agents may be used in or as pharmaceuticals for the treatment of pain, particularly chronic pain.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 15:27:42 ON 27 JUL 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 15:28:13 ON 27 JUL 2002
L1 17833 S (CLOSTRIDIAL TOXIN) OR (CLOSTRIDIAL NEUROTOXIN) OR (BOTULINUM
L2 94674 S (SUBSTANCE P) OR (TRANSMISSION COMPOUND)
L3 4 S L1 (P) L2 (P) (CONJUGATE OR FUSION PROTEIN)
L4 4 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	34.98	35.19

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL

	ENTRY	SESSION
CA SUBSCRIBER PRICE	-2.48	[redacted]8

STN INTERNATIONAL LOGOFF AT 15:31:45 ON 27 JUL 2002